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10/814,195	04/01/2004	Johan Frostegard	FROSTEGARD=1B	6441

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EXAMINER
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COOK, LISA V

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/814,195

**Applicant(s)**

FROSTEGARD, JOHAN

**Examiner**

Lisa V. Cook

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 April 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-12,14 and 15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12,14 and 15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☒ Certified copies of the priority documents have been received in Application No. 09/720,967.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/20/06 has been entered.

### *Amendment Entry*

2. Applicant's response to the Final Action mailed October 19, 2005 is acknowledged (papers filed 3/20/06 and 4/4/06). In the amendments filed therein claims 1, 2, 11, 12, 14, and 15 were modified. Claims 13 and 16-19 have been canceled. Currently claims 1-12 and 14-15 are pending and under consideration.
3. Objections and/or objections of record not reiterated below have been withdrawn.

## NEW GROUNDS OF REJECTIONS NECESSITATED BY AMENDMENT

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-12 and 14-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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A. Claim 1 lines 10-12 are vague and indefinite because it is not clear how the ligand test for phosphocholine, phosphorylcholine, and lysophosphatidycholine relate to the diagnosis of vascular dysfunction or disease. Further, it is not clear how this test is assessed with respect to the measurement of antibodies to PAF. Appropriate correction is required.

B. In claim 1 line 14 it is not clear as to what is being detected. The claim is drawn to the assayed concentration of either or both antibodies to diagnose the condition, however there is no mention of the ligand detection. Accordingly it is not clear if the ligand is detected or not detected? Appropriate correction is required.

C. Claim 2 is vague and indefinite because a correlation step is recited to relate the products with the preamble (diagnosing of early vascular dysfunction and/or vascular disease and/or spontaneous abortion). Please add a correlation step to clarify the claims.

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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I. Claims 1, 5-7, 12 and 14 are rejected under 35 U.S.C.103(a) as being unpatentable over Barquinero et al. (Lupus, 1994, 3, 55-58) in view of Baldo et al. (WO 87/05904) and further in view of Foster et al. (U.S. Patent#4,444,879).

Barquinero et al. teach an ELISA assay to measure antibodies against platelet-activating factor (aPAF) in patients with autoimmune diseases. Antibodies to PAF were measured by binding to PAF. Specifically blood sample from patients with SLE (systemic lupus erythematosus), PAPS (antiphospholip syndrome), and syphilis. SLE is vascular diseases (relating to blood vessels). SLE includes severe inflammation of blood vessels (see The signet Mosby medical encyclopedia definition attached). See abstract and page 55 Introduction and page 56 "ELISA technique for anti-PAF". With respect to the means for determining patients at risk for having cardiovascular disease and/or early atherosclerosis, it is noted that Barquinero et al. teach the measurement of PAF in patients with autoimmune disease such as SLE. SLE includes blood vessel inflammation, which could lead to cardiovascular disease (risk).

Since there is no corresponding structure, etc., in the specification to limit the means step or step plus function limitation, an equivalent is any element that performs the specified function.

Barquinero et al. differ from the instant invention in not specifically teaching a means for testing comprising a ligand selected from the group consisting of phosphorylcholine and lysophosphatidylcholine.

However, Baldo et al. teach antigenic analogues of PAF (ligands) that are used to generate antibodies that bind PAF or antibodies to an antigen that binds aPAF. See claim 1 lines 6-7. The ligands including phosphorylcholine and is disclosed in the examples beginning at page 16 of the disclosure. Lysophosphatidylcholine structures are taught on page 30, for example.

The use of these ligands is taught to be useful because PAF is insufficiently antigenic to produce the necessary PAF-antibodies needed for immunoassay. The novel synthetic analogues (including phosphorylcholine) were sufficient to produce PAF-antibodies, which are suitable for immunoassay of PAF levels in biological fluids. See page 2 lines 4-12.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the ligand phosphorylcholine or lysophosphatidylcholine as taught by Baldo et al. in the measurements of antibodies to PAF and/or antibodies to an antigen(PAF) that binds aPAF as taught by Barquinero et al. because Baldo et al. taught that PAF is insufficiently antigenic to produce the necessary PAF-antibodies needed for immunoassay. The novel synthetic analogues (including phosphorylcholine) were sufficient to produce PAF-antibodies, which are suitable for immunoassay of PAF levels in biological fluids. See page 2 lines 4-12.

Although Barquinero et al. in view of Baldo et al. teach the reagents required by the claims; they do not specifically teach the reagents in kit configurations. In other words, the references fail to teach the reagents as a kit. However, kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example. In their patent kits including the reactant reagents, a microplate, positive controls, negative controls, standards, and instructions are taught. The reagents are compartmentalized or packaged separately for utility. See figure 6, and column 15, lines 10-34.

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It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay reagents as taught by Barquinero et al. in view of Baldo et al. and format them into a kit because Foster et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay. Kits are also economically beneficial in reagent distribution.

II. Claims 2-4, 8-10 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barquinero et al. in view of Baldo et al. and further in view of Foster et al. as applied to claims 1-2 and 5-7 above, and further in view of Ostermann et al. (Thrombosis Research, 52, 529-540, 1988).

Please see Barquinero et al. in view of Baldo et al. and further in view of Foster et al. as set forth above.

Barquinero et al. in view of Baldo et al. and further in view of Foster et al. differ from the instant invention in not specifically teaching PAF and other diagnostic indicators (cholesterol) as indicators for cardiovascular diseases such as atherosclerosis.

However, Ostermann et al. teach PAF quantification in serum and plasma as well as its correlation/diagnosis (discrimination) in Atherosclerotic patients. See abstract and page 531 2<sup>nd</sup> paragraph. Thirty-Six health volunteers and 40 atherosclerotic patients were evaluated in the study. Blood samples were analyzed to determine PAF concentration.

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The results showed a significant increase in serum PAF levels of patients suffering from coronary artery disease. Page 536, last paragraph. The researchers also measured plasma levels. See page 538. Ostermann et al. also teach that PAF could discriminate between low and high-risk groups and was an improvement over other commonly utilized discriminators (total cholesterol, VLDL/LDL-cholesterol, apo). See page 537 2<sup>nd</sup> paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure PAF concentrations in serum and plasma patients with cardiovascular disease such as atherosclerosis as taught by Ostermann et al. in the kit of Barquinero et al. in view of Baldo et al. and further in view of Foster et al. because Ostermann et al. taught the critical role of PAF in myocardial infarction/atherosclerosis and its accuracy of correctly classifying subjects. See abstract. Ostermann et al. further teach that PAF could discriminate between low and high-risk groups and was an improvement over other commonly utilized discriminators (total cholesterol, VLDL/LDL-cholesterol, apo). See page 537 2<sup>nd</sup> paragraph.

One having ordinary skill in the art would have been motivated to do this because the early detection of such disorders is both beneficial in possible prevention and treatment of the disease.

III. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Barquinero et al. (Lupus, 1994, 3, 55-58) in view of Baldo et al. (WO 87/05904) and Foster et al. (U.S. Patent#4,444,879) and further in view of Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Abstract Only).

Please see Barquinero et al. in view of Baldo et al. and Foster et al. as set forth above.



Barquinero et al. in view of Baldo et al. and Foster et al. differ from the instant invention in not specifically teaching a means for testing antibodies comprising phosphocholine.

However, Muzya et al. teach that antibodies involving the ligand phosphatidylcholine (antiphosphatidylcholine antibodies) bind to PAF, lyso-PAF, and acyl analogs of PAF. The binding of antiphosphatidylcholine antibodies to PAF and its structural analogs is related to the presence of phosphocholine fragments. The binding of antiphosphatidylcholine antibodies to PAF was exemplified in the sera of women with obstetrical-gynecological disorders. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use antibodies comprising phosphocholine as taught by Muzya et al. in the method and kit of Barquinero et al. in view of Baldo et al. and Foster et al. because Muzya et al. disclosed that the binding of antibodies to PAF is related to phosphocholine fragments and the measurement of these binding complexes was useful in measuring obstetrical-gynecological disorders in women. See abstract.

### ***Response to Arguments***

6. Applicants contend that the combination of Barquinero et al. and Foster et al. did not disclose the newly amended limitations. This argument was carefully considered and found persuasive. Accordingly the reference of Baldo et al. has been added to teach the added limitations.

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Applicant's arguments against the reference of Karasawa et al. are MOOT because the reference has been removed.

Applicants argue that no motivation exists in Barquinero et al. to employ antibodies other than anti-PAF antibodies. This argument was carefully considered but not found persuasive because Barquinero et al. are cited in combination with Baldo et al. and Baldo et al. disclose the use of antibodies other than anti-PAF antibodies. Specifically Baldo et al. teach antigenic analogues of PAF (ligands) that are used to generate antibodies that bind PAF or antibodies to an antigen that binds aPAF. See claim 1 lines 6-7. One of ordinary skill would have been motivated to use these ligands because Baldo et al. taught that PAF is insufficiently antigenic to produce the necessary PAF-antibodies needed for immunoassay. The novel synthetic analogues (including phosphorylcholine) were sufficient to produce PAF-antibodies, which are suitable for immunoassay of PAF levels in biological fluids. See page 2 lines 4-12.

While a deficiency in a reference may overcome a rejection under 35 USC 103, a reference is not overcome by pointing out that a reference lacks a teaching for which other references are relied. In re Lyons, 364 F.2d 1005, 150 USPQ 741, 746 (CCPA 1966).

In response to the arguments that the use of phosphocholine, phosphorylcholine and/or lysophosphatidylcholine as a ligand provided for a more specific group of antibodies, it is noted that Baldo et al. teach the production of antibodies with these ligands. Accordingly, attorney's arguments of unexpected results cannot take the place of evidence in the record.

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It is also noted that the claims are drawn to a kit (product), therefore there is no requirement that the prior art must suggest that the claimed product will have the same or similar utility as that discovered by applicant in order to support a legal conclusion of obviousness. *In re Dillon*, 919 F.2d 688, 696, 16 USPQ.2d 1897, 1904 (Fed. Cir. 1990). An obviousness rejection is proper under Dillon so long as the prior art suggests a reason or provides motivation to make the claimed invention, even where the reason or motivation is different from that discovered by applicant.

Applicant also contends that the objects in Barquinero and the present invention are different. Specifically, Barquinero does not use aPAF in risk assessment for developing vascular disease. This argument was carefully considered but not found persuasive because the fact that applicant uses the kit for a different purpose does not alter the conclusion that its use would be prima facie obvious from the purpose disclosed in the reference. *In re Lintner*, 173 USPQ 560.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

7. For reasons aforementioned, no claims are allowed.

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*Remarks*

8. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Baldo et al. (LIPIDS, Vol26, No.12, 1991, 1136-1139) teach an immunoassay technique to measure PAF

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 whose telephone number is (571) 272-1600.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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